PAPER

Blood pressure in head-injured patients

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Objective: To determine the statistical characteristics of blood pressure (BP) readings from a large number of head-injured patients.
Methods: The BrainIT group has collected high time-resolution physiological and clinical data from head-injured patients who require intracranial pressure (ICP) monitoring. The statistical features of this dataset of BP measurements with time resolution of 1 min from 200 patients is examined. The distributions of BP measurements and their relationship with simultaneous ICP measurements are described.
Results: The distributions of mean, systolic and diastolic readings are close to normal with modest skewing towards higher values. There is a trend towards an increase in blood pressure with advancing age, but this is not significant. Simultaneous blood pressure and ICP values suggest a triphasic relationship with a BP rising at 0.28 mm Hg/mm Hg of ICP, for ICP up to 32 mm Hg, and 0.9 mm Hg/mm Hg of ICP for ICP from 33 to 55 mm Hg, and falling sharply with rising ICP for ICP >55 mm Hg.
Conclusions: Patients with head injury appear to have a near normal distribution of blood pressure readings that are skewed towards higher values. The relationship between BP and ICP may be triphasic.

Since its introduction in the 1960s,[1] invasive blood pressure (BP) monitoring has become an important part of patient management in high-dependency and intensive care units. Despite widespread use of the modality,[2] few large datasets are available indicating its statistical features. Here we present the results of invasive blood pressure measurements made in 200 patients who were being treated for head injury.

These data have become available as a result of the BrainIT project that was conceived in 1997 and has grown into an international collaboration[3] with the purpose of gathering data on the physiological parameters and treatments associated with significant head injuries with high time resolution. Over the period between 1998 and 2006 data capture systems were deployed in high dependency and intensive-care units of participating neuroscience centres.

The relationship between intracranial pressure (ICP) and BP has been recognised since it was first described by Cushing in 1901.[4] Since then, several reports have confirmed a positive correlation particularly with higher ICPs[5] during tracheal suction[6] and simultaneous with ICP "B waves" in patients being investigated for normal-pressure hydrocephalus.[7] Similar data from 80 patients having computerised monitoring of intra cerebral haemorrhage after head injuries showed a positive correlation for ICPs >25 but not for lower values.[8]

The difference between mean arterial and mean intracranial pressure (cerebral perfusion pressure, CPP) has assumed great importance as it is seen as a parameter for therapeutic optimisation in the care of head-injured patients. Studies have demonstrated the relationship between ICP or CPP and outcome, both in adults[9] and children,[10] alongside the development of guidelines for the management of severe head injury. But any influence on improving outcome has yet to be demonstrated.

We describe the distributions of BP measurements, their relationship with simultaneously taken ICP measurements and the characteristics of the patients in whom the measurements were made.

PATIENTS AND METHODS

The primary goal of the European Union-funded BrainIT project was to collect detailed physiological, clinical and management data from head-injured patients who required ICP and intra-arterial BP monitoring as part of their routine care. In all, 24 participating centres were initially involved in the study. For each centre electronic equipment was provided for minute-by-minute collection of physiological data and also for the input of details of the clinical condition of the patients and management measures used. All data were anonymised before transfer to Glasgow, converted into a standard format and then entered into a database.

Approval for the study was obtained from the relevant local ethical committees and the first patient was recruited in July 2003. Data analyses were performed using Matlab V.6.5. At the time of analysis, a total of 200 patients had been recruited over a period of 24 months from 21 centres. Their age ranged from 4 to 83 years, with a mean (median) of 37 (33) years; 162 were male and 38 female. The causes of injury were: assaultin 17, fall in 56, pedestrian in 16, sport 6, traffic in 85, work in 5 and 15 were unknown.

Presenting Glasgow Coma Scores were available for 184 of the 200 cases and served as an index of injury severity; they ranged from 3 to 15 with a distribution as shown in figure 1. The number of blood pressure measurements per patient varied widely from 52 to 28 584 with the distribution shown in fig 2. Mean BP measurements were available for all patients. A breakdown of these into systolic and diastolic BP was available in 171 patients.

The procedures for managing ICP varied in the different units. But all used some treatment in response to adverse changes in measured pressures. Maintenance of ICP under a threshold value or CPP over a threshold value were both used as therapeutic targets in different patients. ICP thresholds ranged from none to 30 mm Hg and CPP from none to 70 mm Hg. There was also variation in the duration of pressure excursions beyond these thresholds that were seen as significant. This

Abbreviations: BP, blood pressure; CPP, cerebral perfusion pressure; ICP, intercranial pressure

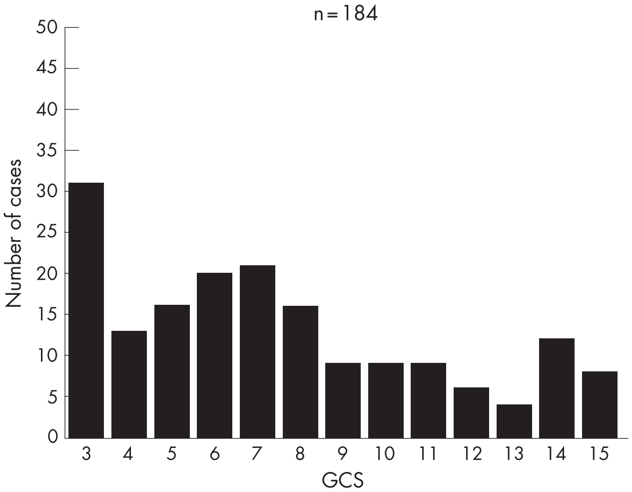

Figure 1 Histogram showing the distribution of pre-neurosurgical hospital Glasgow Coma Score (GCS).

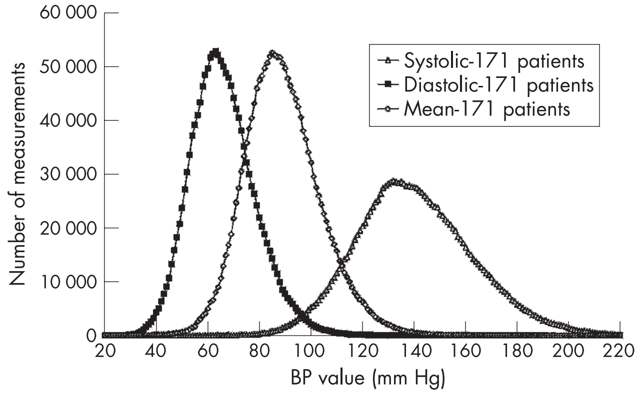

Figure 3 Line plots showing the distributions of diastolic, systolic and mean invasive blood pressures (BP) measurements.

variation reflects the ongoing debate about the best way to manage raised ICP after head injury.

Some artefactual measurements are to be expected in a dataset of this type. To minimise the inclusion of these readings, measurements outside the credible physiological ranges were excluded. The distribution of measurements was observed and compared with the expected smooth distribution of natural phenomena. The data contain what appears to be a substantial over-representation of values of ICP between 0 and −20 mm Hg and of BP values below 20 mm Hg. These values were excluded because it was assumed that a majority, though not all, were artefactual.

The statistical methods used are mainly descriptive. The points plotted in the figures represent mean values of BP. Confidence limits were calculated using Poisson distributions. The overall closeness of the distribution of BP data to a normal distribution was assessed using quantile–quantile (Q-–Q) plots where the quantiles of the dataset were plotted on the x axis against quantiles of a theoretical normal distribution with the same mean and variance on the Y axis (fig 4). Standardised third moments were calculated to give a quantitative measure of the amount of skew in the distributions. Least squares linear regression was used on the dataset presented in fig 5 to express BP as a function of ICP over two regions that were identified by visual inspection of the graph.

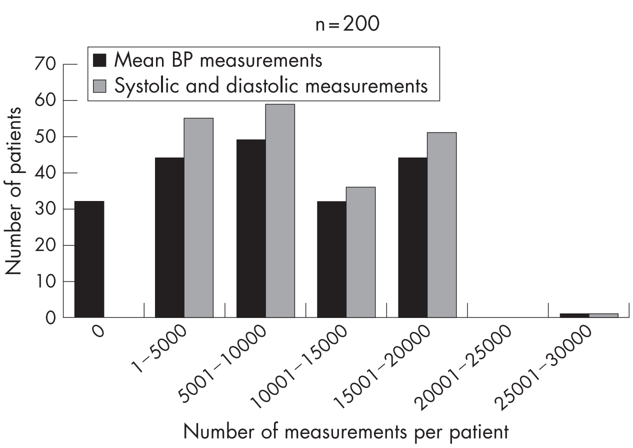

Figure 2 Histogram showing the distribution of observations per patient. The distinction between mean blood pressure measurements (BP) and systolic and diastolic measurements is a consequence of different types of data collection systems. All systems that collect systolic and diastolic measurements also calculate means but some only given means and not a systolic and diastolic breakup.

RESULTS

BP distributions

The dataset included 1.6, 1.6 and 1.8 million observations of diastolic, systolic and mean blood pressures, respectively. The distributions of these measurements are shown graphically in fig 3 and summary statistics are given in table 1. All three distributions are close to normal as can be seen in fig 3. Further analysis with Q–Q plots (fig 4) shows that none of the distributions are quite normal, all being skewed towards higher values.

Relationship between BP and ICP

BPs may be higher on average in head-injured patients than in others. The association between head injury and raised ICP may produce a reflex hypertension and in some cases therapeutic hypertension is used as a treatment for raised ICP. Simultaneous data on BP and ICP are available in the BrainIT dataset from 195 patients and shows the relationship between mean intracranial pressure and mean BP (fig 5). There is wide variation in the number of measurements made at different values of ICP which reflects the relative rarity of readings at >35 mm Hg. The distribution of the number of simultaneous BP and ICP measurements as a function of both BP and ICP demonstrated a two-directional normal distribution with slight skewing towards high ICP and BP values.

Relationship between BP and age

It is well recognised that BP rises with advancing age. A scatter plot of BP versus age for the patients in this series is shown in fig 6. The slight trend towards an increase in BP with advancing age did not reach significance. The 95% limits of the linear

Table 1 Means and SDs of invasive blood pressure data (mm Hg)

Blood pressure	Mean	SD	Standardised third moment	No of observations.
Systolic	140.41	23.10	0.36	1 557 767
Diastolic	66.21	13.78	2.10	1 556 760
Mean	89.43	16.23	1.74	1 814 850

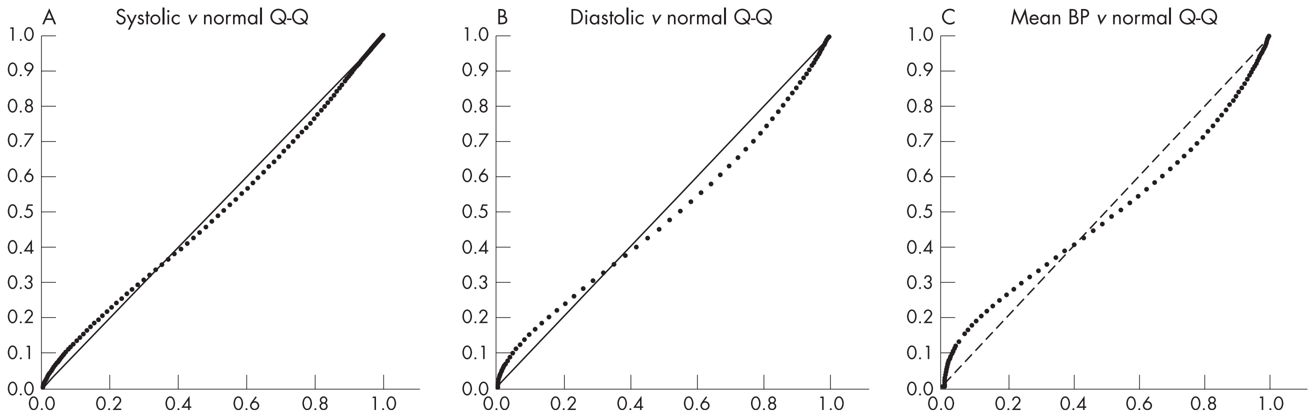

Figure 4 Q–Q plots of the distributions of systolic (A), diastolic (B) and mean (C) blood pressures. In a Q–Q plot the quantiles measured from the dataset are plotted against the theoretical quantiles of a normal distribution that has the same mean and SD as the dataset. A perfectly normally distributed dataset will have a Q-Q plot along the straight line. The sigmoid deviation from the straight line seen in the three plots, most prominently in the mean plot, indicates skewing towards higher blood pressures.

relationship between patient age and BP, and of the individual values are also shown in fig 6.

Artefacts

Certain features of the dataset suggest artifactual over-representation of particular values. The distribution of mean BP observations in the range of 100–30 mm Hg shows peaks of numbers of observations at 91, 40, 19 and 4 mm Hg. These numbers clearly do not represent true physiological measurements. There is a large peak of 9784 data points at the BP = 0, which is suspected to be an artefact. These artefactual measurements are excluded from the data presented in figs 3–6 and table 1. In the case of ICP measurements, there is a peak at 0 mm Hg of ICP, which is believed to be an artefact. It is suspected that the values of 1, 2, 3 and 4 mm Hg ICP are also over-represented in the dataset. This is indicated by distortion of the distribution of ICP values and also by the first four points on the graph of ICP versus BP (fig 5).

DISCUSSION

The BrainIT dataset is one of the largest of high time-resolution invasive BP in head injury. It was collected in a large number of units from different European countries. Certain features of data-distribution analyses such as small deviation from a normal distribution can only be determined from large datasets.

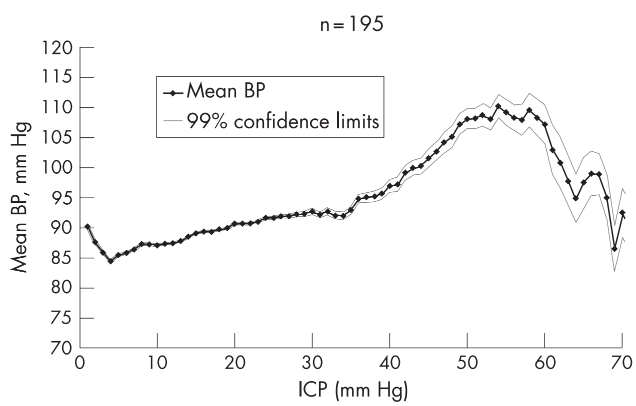

Figure 5 The relationship between intracranial pressure (ICP) and blood pressure (BP). Limits of 99% were chosen because 95% limits are too narrow to be resolved over most of the graph. The CIs are of the means and are based on Poisson distributions.

The measurements made in head-injured patients should be applied to other patients with caution. The relationship between mean ICP and mean BP shown in fig 5 extends over the range of ICP that would normally be regarded as ''normal'' of between 0 and 15 mm Hg.[11 12] Even a population of patients with head injuries and relatively normal ICP may have a slightly raised BP consequent upon changes in ICP within the normal range.[13] Furthermore, the effects of the post-traumatic stress response and sedation may have influenced the results.

The graph in fig 5 appears to naturally fall into four zones: for ICP values between 4 and 32 mm Hg, BP is related by the equation:

$$BP = 0.28 * ICP+84.4$$

for ICP between 33 and 55 mm Hg the equation changes to

$$BP = 0.90 * ICP+61.6.$$

The upswing in the BP values at ICPs of 0, 1, 2 and 3 mm Hg may be an artefact as ICP measurements with these low values are over-represented in the dataset. The over-representation is believed to be quasi-randomly distributed in the dataset. This means that the greater the proportion of artefactual readings at a specific value, the nearer the average BP at the value will be to the overall average. This may explain the initial down slope. If this were the full explanation, the mean BP with ICP = 0 would be expected to be just under the overall average of 89.29 mm Hg, but is 92.04 mm Hg. It is interesting to note that the same down slope in BP for the range of ICP from 0 to 3 can be seen in the data reported by Czosnyka *et al*.[8] The decline in BP over ICP of 55 mm Hg is probably real and reflects the fact that most cases under these circumstances are suffering from agonal coning.

The relationship between ICP and BP in fig 5 shows a tendency to maintain CPP at or above 60 mm Hg. There may be an iatrogenic component to this as maintenance of ICP or CPP were used as therapeutic targets. Physiological effects cannot be distinguished from the effects of treatment aimed at optimising ICP, BP or CPP because patients were selected to receive such treatment on the grounds of changes in the same parameters. It is not possible to separate treatment effects from selection effects in a dataset of this type but it is likely that for ICPs <20 mm Hg the effect seen is physiological, because there is

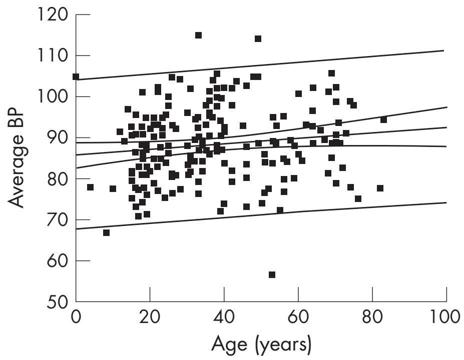

Figure 6 Scatter plot of patient age versus mean blood pressure (BP) for individual patients. The 95% limits of the mean and values are shown. The slight positive relationship does not reach significance.

little reason to pharmacologically increase BP in response to ICP in this region. Of note is that contrary to the findings of Czosnyka *et al*,[8] we have observed a positive correlation between ICP and BP over this region.

CONCLUSIONS

Based on invasive BP measurements in 200 head-injured adult patients the distribution of BP is not normal but skewed towards high values. The means (and SD) of diastolic, systolic and mean measurements were 66 (13.8), 140 (23.2) and 89 (16.5) mm Hg, respectively.

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PM, BAG, ADM and IRC conceived the analysis. PM, BAG and IRC performed the analysis. PM, BAG, IP, GC, ADM and IRC helped draft the manuscript. IP, BAG, GC and IRC are on the Steering Committee of BrainIT. All authors have had access to all of the data in the study and they held final responsibility for the decision to submit for publication.

REFERENCES

1 **Bevan AT**, Honour AJ, Stott FH. Direct arterial pressure recording in unrestricted man. *Br Heart J* 1969;**31**:387–8.
2 **Pinsky MR**. Hemodynamic monitoring in the intensive care unit. *Clin Chest Med* 2003;**24**:549–60.
3 **BrainIT**. Neurointensive care monitoring research group, 1998. URL, http://www.brainit.org (accessed 24 January 2003).
4 **Cushing H**. Some experimental and clinical observations concerning states of increased intercranial tension. Mutter Lecture, 1901.
5 **Gobiet W**, Grote W, Bock WJ. The relation between intracrainal pressure, mean arterial pressure and cerebral blood flow in patients with severe head injury. *Acta Neurochir Wien* 1975:13–24.
6 **Wang MH**, Cheng SY, Wang YC, *et al*. The effect of intracranial pressure caused by airway suction in hypertensive intracerebral hemorrhagic comatose patients. *Zhonghua Yi Xue Za Zhi Taipei* 1993;**52**:109–15.
7 **Droste DW**, Krauss JK. Intracranial pressure B-waves precede corresponding arterial blood pressure oscillations in patients with suspected normal pressure hydrocephalus. *Neurol Res* 1999;**21**:627–30.
8 **Czosnyka M**, Price DJ, Williamson M. Monitoring of cerebrospinal dynamics using continuous analysis of intracranial pressure and cerebral perfusion pressure in head injury. *Acta Neurochir Wien* 1994;**126**:113–19.
9 **Chambers IR**, Treadwell L, Mendelow AD. Determination of threshold levels of cerebral perfusion pressure and intracranial pressure in severe head injury by using receiver-operating characteristic curves: an observational study in 291 patients. *J Neurosurg* 2001;**94**:412–16.
10 **Chambers IR**, Jones PA, Lo TYM, *et al*. Critical thresholds of intracranial pressure and cerebral perfusion pressure in paediatric head injury related to age. *J Neurol Neurosurg and Psychiatry* 2006;**77**:234–40.
11 **Williams B**. Simultaneous cerebral and spinal fluid pressure recordings. I. Technique, physiology, and normal results. *Acta Neurochir Wien* 1981;**58**:167–85.
12 **Shapiro K**, Marmarou A, Shulman K. Characterization of clinical CSF dynamics and neural axis compliance using the pressure-volume index: I. The normal pressure-volume index. *Ann Neurol* 1980;**7**:508–14.
13 **Schmidt EA**, Czosnyka Z, Momjian S, *et al*. Intracranial baroreflex yielding an early Cushing response in human. *Acta Neurochir Suppl* 2005;**95**:253–6.